衛生福利部疾病管制署

孕婦與新生兒愛滋感染及愛滋抗藥性問題

衛福部 疾病管制署
中區傳染病防治醫療網
王任賢 指揮官

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Mother To Child Transmission of HIV (MTCT)

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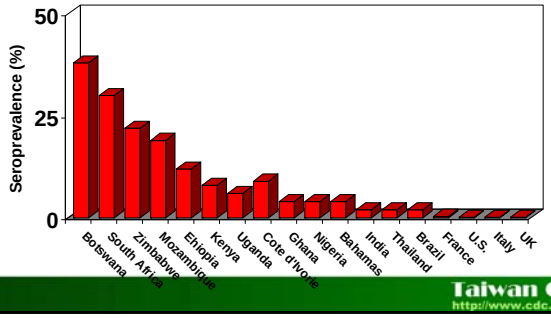
HIV Seroprevalence Among Pregnant Women in Selected Developed & Developing Countries

WHO, Africa 2004, others 2002-2003



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Mother to Child Transmission

- MTCT in developed nations was 15 – 30 % (prior to ARVs)
- MTCT in resource limited settings is 25 - 45%
- Breast Feeding (BF) increases the risk of MTCT by 5 - 20% depending on the status of the breasts, length of BF, immune status of mother and her infant
- Vertical Transmission occurs
  - In utero - 10 – 20%
  - Intrapartum - 50 – 60%
  - Postpartum (PP) through BF – 20 - 40%

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Risk Factors for MTCT

- Maternal plasma, RNA, viral load
- Maternal immune status – CD4 cell count
- Cervico-vaginal infection and STDs
- Mode of delivery – vaginal delivery is associated with higher transmission
- Prolonged rupture of membranes
- Breastfeeding doubles the rates of transmission especially where breastfeeding continues in the 2nd year

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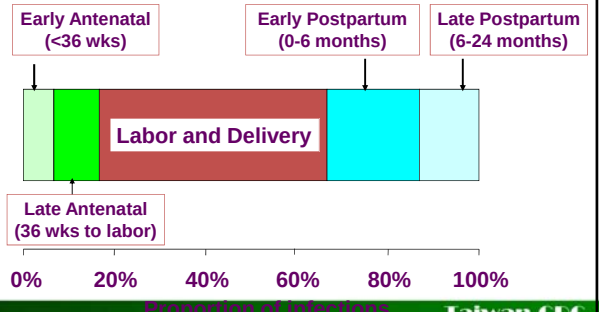
Timing of Mother-to-Child HIV Transmission with Breastfeeding & No Antiretroviral Prophylaxis



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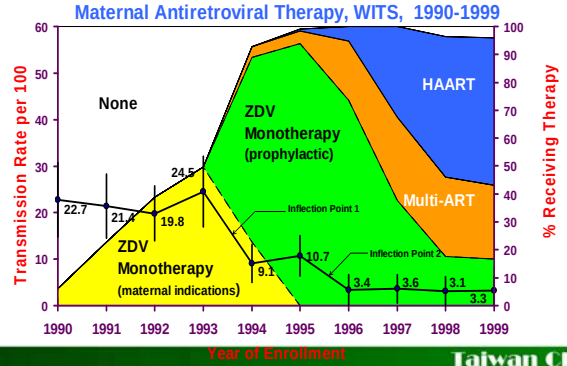
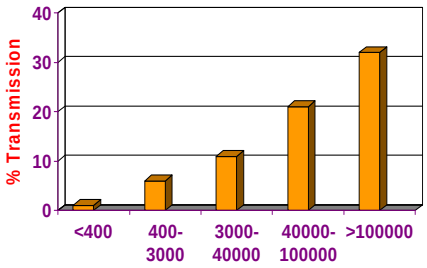
Trends in Mother-to-Infant Transmission Rate and Maternal Antiretroviral Therapy, WITS, 1990-1999

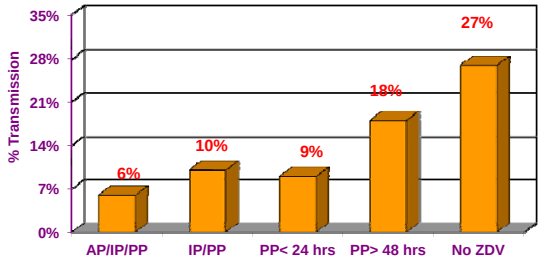


Delivery Plasma HIV RNA Levels and Perinatal Transmission in WITS, 1990-1999

Blattner W. XIII AIDS Conf, July 2000, Durban S Africa (LBOr4)

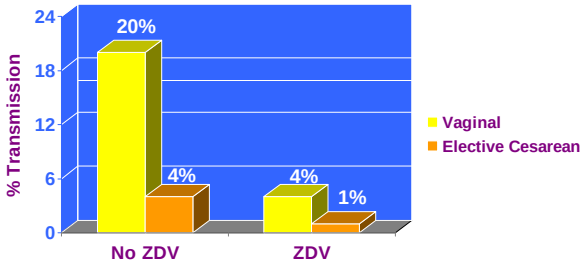


ZDV Components and Perinatal Transmission of HIV



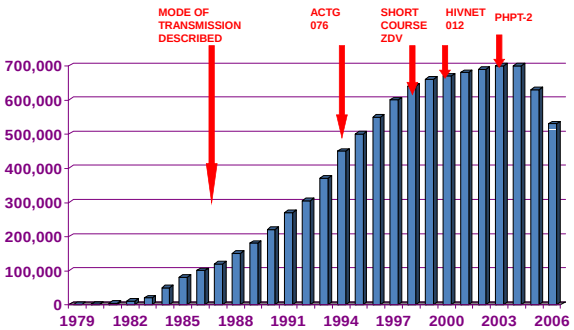
Wade, NEJM 1998;339:1409

European Randomized Mode of Delivery Trial: Elective Cesarean at 38 Weeks vs Vaginal Delivery



Lancet 1999;353:1035-9

Mother-to-Child Transmission (MTCT) of HIV Estimated Children Newly Infected in World



UNAIDS estimates

Mode of Breast feeding and HIV transmission

- Modes of infant feeding — Rates of VT at 15 m
  - Infants formula fed - 19%
  - Infant breast fed exclusively - 25%
  - Infants mixed fed - 36 %
- Exclusive B/F provides some degree of protection from HIV breast milk transmission

Coutsoudis A et al AIDS 2001

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Prevention of Mother To Child Transmission of HIV (PMTCT)

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Strategies for PMTCT

1. Primary prevention of HIV among parents to be
   - Abstinence before marriage
   - Fidelity for married couples
   - Use of condoms if 1 and 2 fail (ABC)
2. Prevention of unwanted and unintended pregnancy among HIV infected women
   - Preconception Counseling and Testing
   - Family Planning – Dual method
   - Community mobilization and education
3. Prevention of transmission from HIV infected women to their infant
4. Provision of treatment, care and support of HIV infected women, their infants and their families

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Intervention Package

- Access to ANC for all pregnant women
- Routine counselling and testing for all ANC mothers
- Comprehensive ANC improved care during labor and delivery and postpartum care
- Infant feeding counseling and training
- Modified obstetric practices
- Antiretroviral therapy during pregnancy and breastfeeding
- Exclusive breastfeeding for not more than 6 months
- Replacement feeding for HIV+ mothers who opt not to breastfeed
- Promotion of community and family support

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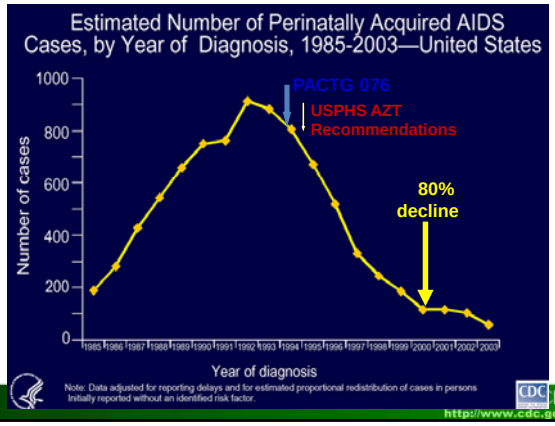

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ARVs in the Prevention of Vertical Transmission

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ACTG 076 – 1990 - 1994

ACTG 076 was a placebo controlled trial

- AZT was given to HIV+ Pregnant women
- Oral AZT 100mg 5xday starting at 14 weeks
- IV AZT in labor
- Oral AZT to both Mother and Infant for 6 wks Postnatal - No breast feeding

1994 RESULTS	HIV TRANSMISSION
Placebo	25%
AZT	8%

66% Reduction - Cost $1000

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CDC Thai - 1996 -1998

- Oral AZT 300 mg 2xday starting at 36 weeks gestation
- Oral AZT 300mg 3 hourly during labor
- No postnatal drugs
- No breastfeeding of infants

1998 RESULTS	HIV TRANSMISSION
Placebo	18.6%
AZT	9.2%

50% Reduction - Cost $90

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PETRA – 1996 – 2000 (WHO)

- Petra trial (PETRA = Perinatal Transmission) was carried out in 5 sites, Mulago and Nsambya - Uganda, Dar es Salaam - Tanzania, and Durban and Johannesburg - South Africa
- Used two drugs 300mg AZT (ZIDOVUDINE) + 150mg 3TC (LAMUVIDINE) 2 x day in combination orally, in a breastfeeding population

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PETRA – 1996 – 2000 (WHO)

There were 4 different arms

- ARM A = tab AZT + 3TC bd starting 36wks to labor, then same drugs 3 hourly in labor and bd to mother and baby for 1 wk after delivery reduced transmission by 61%
- ARM B = Same regimen as in ARM A without antenatal dosing reduced transmission by 37%
- ARM C = Same regimen as ARM A given only in labor - No reduction of transmission
- ARM D = Placebo – No reduction of transmission
- Cost - $150

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HIVNET 012 (Nevirapine Study) (1997 – 1999)

Study Objective:

To compare the use of

oral NVP versus oral AZT

given to the mother in labor and to the infant after delivery

to prevent MTCT of HIV in pregnant HIV infected women

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Study Population

620 HIV infected pregnant women

310 WOMEN
NEVIRAPINE (NVP)

Mother (200mg At labor onset)

Infant (2mg/kg within 72 hrs)

310 WOMEN
ZIDOVUDINE (AZT)

Mother (600mg at labor onset, then 300mg 3hrly till delivery)
Infant (4mg/kg Bid for 1 week)

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Infant Results

- Infant HIV results at 14 wks (HIV RNA-PCR)
  - NVP arm: 13% transmission
  - AZT arm: 26% transmission
  - 50% reduction of HIV MTCT in NVP arm
- Drugs were safe and well tolerated
- No side effects related to drugs
- **INFANTS**: 18 months HIV ELISA; 60 months safety data

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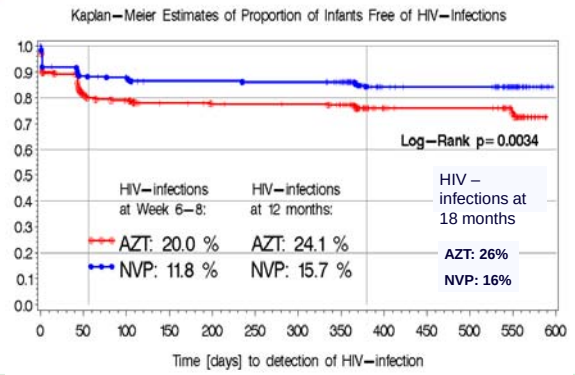
HIV TRANSMISSION THROUGH 18 MONTHS



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Nevirapine Resistance after a single dose of NVP

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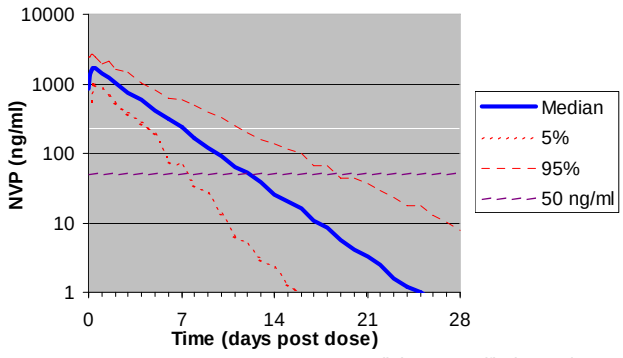
Simulated NVP Concentrations Following Single Dose NVP Intrapartum Administration

Cressey TR et al.

JAIDS 2005;38:283-8



Lower limit assay quantification 50 ng/mL

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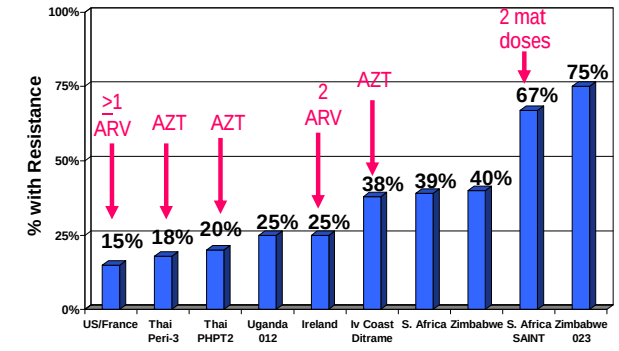
Summary: Acquisition of NVP Resistance in Mothers Following NVP Prophylaxis



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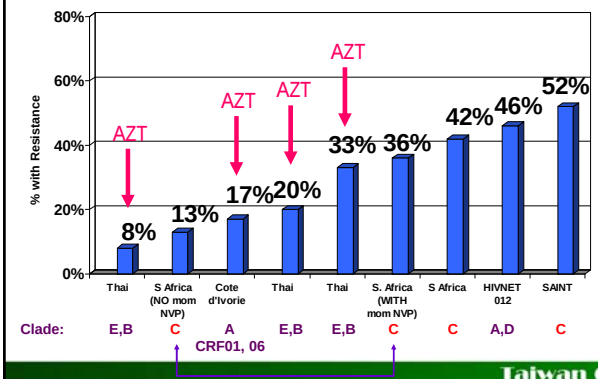
Summary: Acquisition of NVP Resistance in Infants Following SD NVP Prophylaxis



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What are the implications of resistance following NVP use for PMTCT?

- Impact on transmission:
  - current pregnancy?
  - subsequent pregnancies?
  - sexual partners?
- Impact on future maternal treatment options?

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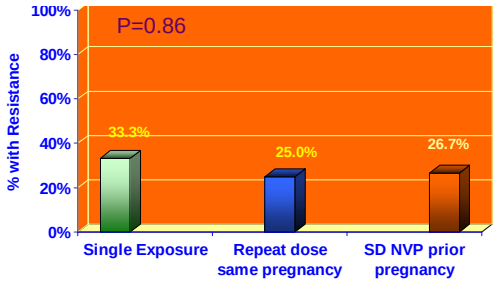
Nevirapine in subsequent pregnancies

- Effectiveness of NVP in a second pregnancy shown in Soweto (10.2%) and Abidjan (3%) (Martinson, CROI 2006)
- Data from Kampala show similar efficacy of sdNVP in women who have previously received NVP as women receiving it for the first time (14.6% vs 17.6%) (CROI 2006)

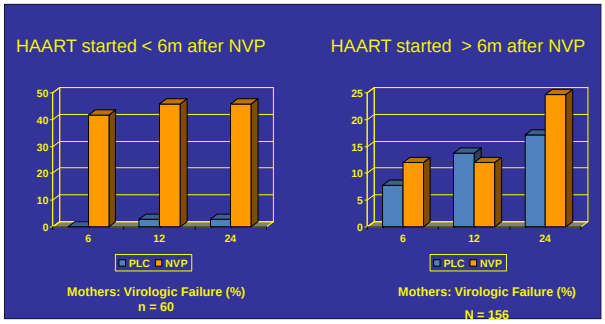
NVP Resistance is Not Increased in Women with Repeat Exposure to SD NVP for PMTCT

Kuhn L et al. JAIDS 2006;42:260-3



Odds of resistance with repeat exposure adjusting for RNA, CD4 and time sample: OR 1.06; 95% CI 0.2-5.6

Does prior NVP use for PMTCT impact on the use of NVP-containing HAART?



Lockman et al. 43rd Annual Meeting of IDSA, October 6 – 9 2005, San Francisco, LB-5

Reducing NVP Resistance after sdNVP to mother

- TOPS study – S. Africa (McIntyre – CROI 2005)
  - Addition of 4 -7 days of AZT + 3 TC postnatally to mother and infant
  - Reduced maternal NVP resistance from 50% to 10%
- Ditrame 1.1 – West Africa (F Dabis CROI 2005)
  - Addition of 3 days of AZT + 3TC postnatally to mother
  - Reduced maternal NVP resistance from 28 % to 1.1 %

Improving Effectiveness of Nevirapine Regimen – WHO Recommendations

Recent WHO Guidelines for use of ART for PMTCT: I

- Basic regimen
  - Single dose Nevirapine (sdNVP) for mother at onset of labor and baby within 72hrs after delivery – 6%
- Combination regimen
  - AZT + 3TC given twice daily starting from 32 – 36 weeks. Combined with sdNVP at onset of labour and baby within 72hrs and AZT twice daily for 1 week for the baby – 5%
  - AZT given twice daily starting at 28-32 weeks through labour and boosted by sdNVP at onset of labor and to baby within 72 hrs and AZT twice daily for 1 week – 6%

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Recent WHO Guidelines for use of ART for PMTCT: II

- HAART – pregnant women eligible for HAART will be given AZT+3TC+NVP starting at 14 weeks or later for life and baby receives AZT 4mg/kg body weight for 1 week – <2%
- All HIV+ women from PMTCT will be followed up with their family in PMTCT Follow-up clinic and initiate HAART when it is necessary

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Prolonged Infant Antiretroviral Prophylaxis For Prevention of Breast Milk Transmission

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Prevention of HIV transmission thru BF

SIMBA study (Rwanda and Uganda – BF populations)

- Maternal AZT + DDI from 36 wks to delivery and 1 wk PP
- Infant prophylaxis with NVP or 3TC for the breast feeding period (randomized)
- Median duration of breast feeding about 3.5 months
- Reduced transmission of HIV thru BF in both arms
- Preliminary results show only 1% postnatal transmission in first 3 months
- Overall transmission was 10%

Vyankandondera et al. IAS Paris 2003 abstract

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SIMBA – NVP vs 3TC infant prophylaxis

- 405 HIV+ women from Rwanda and Uganda
- Maternal AZT + DDI from 36 weeks gestation
- Infants randomized to NVP or 3TC during breastfeeding
  - 198 NVP and 199 3TC
  - Only 7 infants infected in the 3TC and NVP arms (excluding those + at birth) by 6 months of ag
  - No difference between the NVP vs 3TC arms

Vyankandondera J et al. IAS Paris, France 2003

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